Updated Guidelines for Managing Menopausal Symptoms

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- There are no relevant financial relationships with any commercial interests to disclose
Key Points:
Position Statement
on Hormone Therapy

*Menopause* 2012; 19 (3): 257-271

Available at: menopause.org

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**NAMS Definitions**

<table>
<thead>
<tr>
<th>Acronym</th>
<th>Full name</th>
</tr>
</thead>
<tbody>
<tr>
<td>ET</td>
<td>Estrogen (E) therapy</td>
</tr>
<tr>
<td>EPT</td>
<td>Combined E+P therapy</td>
</tr>
<tr>
<td>HT</td>
<td>Hormone therapy (ET, EPT)</td>
</tr>
<tr>
<td>MHT</td>
<td>Menopausal hormone therapy</td>
</tr>
<tr>
<td>Progestogen</td>
<td>Progesterone or progestin (P)</td>
</tr>
<tr>
<td>CC-EPT</td>
<td>Continuous-combined E+P therapy</td>
</tr>
<tr>
<td>CS-EPT</td>
<td>Continuous-sequential E+P therapy</td>
</tr>
</tbody>
</table>

## Abbreviations/Definitions

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>E</td>
<td>Estrogen</td>
</tr>
<tr>
<td>$E_2$</td>
<td>Estradiol</td>
</tr>
<tr>
<td>CEE</td>
<td>Conjugated Equine Estrogen</td>
</tr>
<tr>
<td>P</td>
<td>Progesterone</td>
</tr>
<tr>
<td>P</td>
<td>Progestin</td>
</tr>
<tr>
<td>P</td>
<td>Progestogen (refers to either progesterone or progestin)</td>
</tr>
</tbody>
</table>

### Act 1

*Let’s Get This Out of the Way....*

*The WHI Re-analyzed*
**Women’s Health Initiative (WHI)**

- **1993-2005:** RCT with 17,000 women
- **Postmenopausal women 50-79 years old**
  - 33%: 50-59 yrs old; 45%: 60-69 yo; 22% 70-79 yo
  - **Average age: 64 years old**
- **End points**
  - Primary prevention of MI and stroke
  - Hip fracture, various cancers
- **Treatment arms**
  - If uterus: CC-EPT (CEE+MPA) vs. placebo
  - If no uterus: ET (CEE) vs. placebo

### WHI: EPT Arm Study Results
**Released July 2002: Findings after 5.2 years**

<table>
<thead>
<tr>
<th>Event</th>
<th>RR</th>
<th>Attributable Risk /10K/yr</th>
<th>Attributable Benefit /10K/yr</th>
<th>Number needed to harm or benefit/year</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart attack</td>
<td>1.29</td>
<td>7</td>
<td></td>
<td>1,100</td>
</tr>
<tr>
<td>Stroke</td>
<td>1.41</td>
<td>8</td>
<td></td>
<td>1,200</td>
</tr>
<tr>
<td>Breast CA</td>
<td>1.26</td>
<td>8</td>
<td></td>
<td>1,300</td>
</tr>
<tr>
<td>TE event</td>
<td>2.11</td>
<td>18</td>
<td></td>
<td>600</td>
</tr>
<tr>
<td>Colorectal cancer</td>
<td>0.63</td>
<td>6</td>
<td></td>
<td>1,700</td>
</tr>
<tr>
<td>Hip fractures</td>
<td>0.66</td>
<td>5</td>
<td></td>
<td>2,000</td>
</tr>
</tbody>
</table>

Discontinued early, as “risks greater than benefits”
The Women’s Health Initiative

– *Was* a drug study of the effect of hormones on CVD, cancer, fractures, and memory in older women (mainly in 60s, long post-menopausal)

– *Was not* a menopause study...
  - Only 3.5% subjects were “early menopause”
  - Excluded symptomatic menopausal women
**WHI: HT and Risk of CV Disease by Age and Years Since Menopause**

Roussow JE. *JAMA*. 2007: Combined secondary analysis

<table>
<thead>
<tr>
<th>Age at HT initiation</th>
<th>Heart attack</th>
<th>Stroke</th>
<th>Death from any cause</th>
</tr>
</thead>
<tbody>
<tr>
<td>50–59 years</td>
<td>↓ 7%</td>
<td>↑ 13%</td>
<td>↓ 30%</td>
</tr>
<tr>
<td>60–69 years</td>
<td>↓ 2%</td>
<td>↑ 50%</td>
<td>↑ 5%</td>
</tr>
<tr>
<td>70–79 years</td>
<td>↑ 26%</td>
<td>↑ 21%</td>
<td>↑ 14%</td>
</tr>
</tbody>
</table>

“Women who initiated HT closer to menopause tended to have reduced CHD risk compared with the increase in CHD risk among women more distant from menopause, but this trend test did not meet our criterion* for statistical significance.”

*Statistically significant defined as $p<0.01$.

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**HT and CVD: The Unified Hypothesis**

HT & Breast Cancer

- EPT use >4-5 years increased breast cancer risk
  - Increased absolute risk of EPT in WHI: “rare”
  - 4-6 additional cases/10,000/yr of EPT for ≥ 5 yrs
- Estrogen only regimens
  - WHI ET trial showed no increased risk after 7.1 yrs
    - 6 fewer cases/10,000 women/yr of ET use
  - Other studies showed that ET for < 5 yrs has little or no impact on breast cancer risk


Menopausal Hormone Therapy for the Primary Prevention of Chronic Conditions

USPSTF 2012

- The USPSTF recommends against the use of
  - EPT for prevention of *chronic conditions* in postmenopausal women
    - Grade: D Recommendation
  - ET for the prevention of *chronic conditions* in postmenopausal women who have had a hysterectomy
    - Grade: D Recommendation
Therapeutic Interventions

- Lifestyle changes
- Botanicals and PhytoSERMs
- Non-hormonal Rx medications
- Hormone Therapy (MHT)

Symptoms of Estrogen Deficiency

- Vasomotor symptoms (VMS) → hot flashes, night sweats
- Neuro-behavioral changes → short term memory loss
- Bone loss → increased hip, vertibral fracture risk
- Vaginal atrophy → vaginal dryness, dyspareunia, urge incontinence
**VMS Characteristics**

- Experienced by 75% percent of menopausal women
  - May start during the peri-menopause
  - On average last for 2 years, then wane
  - 25% have hot flushes > 5 years after menopause
- Ethnic and racial differences
  - More common in African-American women
  - Less common in Chinese, Japanese women
- Smoking and obesity are risk factors


**Management of VMS: Lifestyle Changes**

- Cool room temperature
- Dress in layers
  - Remove outer layers if warm
- Exercise routinely, at least 3-4 days/week
- Avoid triggers
  - Hot and spicy foods
  - Cigarettes
  - Alcohol

**Botanicals and PhytoSERMs**

*Probably better than placebo*
- Black cohosh

*No evidence of efficacy*
- Soy isoflavones  Not better than pbo
- Red clover isoflavones  Not better than pbo
- Evening primrose oil  Not better than pbo
- Dong quai  Not better (as monotx)
- Ginseng  Not better than pbo
- Vitamin E  Not better than pbo
- Chasteberry (Vitex)  No studies

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**Botanicals: Black Cohosh**

- 14 trials reported, including 4 randomized trials using placebo and/or estrogen treatment arm
  - 3 of 4 RCTs found black cohosh to be beneficial
  - 12 of 14 trials reported *some* benefit
  - Currently, longest trial is 6 months
- NIH, large, randomized, prospective, 2-year trial
  - Preliminary data fail to show binding to E receptors
  - Binding to serotonin receptor noted
Botanicals and PhytoSERMs

- Positive effect of black cohosh vs placebo
  - Improvement is less than with estrogen
- Some of the impact is due to placebo effect, which is none-the-less therapeutic
- Relatively little risk of adverse effects
- **Reasonable first-line choice for women**
  - With mild menopausal symptoms
  - Who feel strongly about avoiding hormones
  - Who are willing to use medications that are not “proven” effective by EBM or regulated by FDA

Non-Hormonal Hot Flash Therapies

<table>
<thead>
<tr>
<th>Medication</th>
<th>% treated patients with &gt;50% ↓HF</th>
<th>% placebo patients with &gt;50% ↓HF</th>
</tr>
</thead>
<tbody>
<tr>
<td>Venlafaxine</td>
<td>54-70%</td>
<td>30%</td>
</tr>
<tr>
<td>Paroxitine</td>
<td>50-76%</td>
<td>35-57%</td>
</tr>
<tr>
<td>Sertraline</td>
<td>40-56%</td>
<td>21-41%</td>
</tr>
<tr>
<td>Gabapentin</td>
<td>46-84%</td>
<td>27-47%</td>
</tr>
<tr>
<td>Escitalopram</td>
<td>55%</td>
<td>36%</td>
</tr>
</tbody>
</table>

J Clinical Oncology June, 2009
VMS: Paroxetine 7.5 mg

- Most commonly used SSRI is paroxetine
- Brisdelle™ is the only FDA-approved nonhormonal therapy to treat VMS
- Most common adverse reactions vs. placebo
  - Headache
  - Fatigue/malaise/lethargy
  - Nausea/vomiting

VMS and Gabapentin (GBP)

<table>
<thead>
<tr>
<th>Author</th>
<th>Dose</th>
<th>% HF↓ GBP</th>
<th>% HF↓ Placebo</th>
<th>% HF↓ Estrogen</th>
</tr>
</thead>
<tbody>
<tr>
<td>Butt DA 2008</td>
<td>300 mg TID</td>
<td>51%</td>
<td>26%</td>
<td>NA</td>
</tr>
<tr>
<td>Guttuso TJ 2003</td>
<td>900 → 2700 mg</td>
<td>54%</td>
<td>31%</td>
<td>NA</td>
</tr>
<tr>
<td>Pandya KG 2005</td>
<td>300 mg TID</td>
<td>46%</td>
<td>18%</td>
<td>NA</td>
</tr>
<tr>
<td>Reddy SY 2006</td>
<td>Up to 2400 mg (800 mg TID)</td>
<td>71%</td>
<td>54%</td>
<td>72%</td>
</tr>
</tbody>
</table>
### Prescription HT Options: ET and EPT

<table>
<thead>
<tr>
<th>Oral</th>
<th>Transdermal</th>
<th>Intravaginal</th>
</tr>
</thead>
</table>
| **ET** | • Micronized estradiol  
• Conjugated equine estrogens (CEE)  
• Synthetic conjugated estrogens  
• Esterified estrogens  
• Estropipate  
• Estradiol acetate | • Patches  
• Gels  
• Emulsion  
• Spray | • Creams  
• Intravaginal tablet  
• Rings |
| **EPT** | • CC-EPT  
• CS-EPT | • E+P combination patches |

### Hormone Therapy Regimens

<table>
<thead>
<tr>
<th>Month 1</th>
<th>Month 2</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Estrogen Therapy (ET)</strong></td>
<td><strong>Estrogen Therapy (ET)</strong></td>
</tr>
<tr>
<td><strong>Estrogen</strong></td>
<td><strong>Estrogen</strong></td>
</tr>
<tr>
<td>Continuous combined (CC) EPT</td>
<td>Continuous combined (CC) EPT</td>
</tr>
<tr>
<td><strong>Estrogen</strong></td>
<td><strong>Estrogen</strong></td>
</tr>
<tr>
<td><strong>Progestin</strong></td>
<td><strong>Progestin</strong></td>
</tr>
<tr>
<td>Continuous-sequential (CS) EPT</td>
<td>Continuous-sequential (CS) EPT</td>
</tr>
<tr>
<td><strong>Estrogen</strong></td>
<td><strong>Estrogen</strong></td>
</tr>
<tr>
<td><strong>Progestin 14d</strong></td>
<td><strong>Progestin 14d</strong></td>
</tr>
<tr>
<td>Off for 14 d</td>
<td>Off for 14 d</td>
</tr>
<tr>
<td>Continuous-pulsed (CP) EPT</td>
<td>Continuous-pulsed (CP) EPT</td>
</tr>
<tr>
<td><strong>3d</strong></td>
<td><strong>3d</strong></td>
</tr>
</tbody>
</table>
Choice of HT Regimen

• If no uterus: ET only
• If uterus present
  – Goal is to avoid vaginal bleeding entirely, or, at least, to make it predictable
• Endometrial activity predicts bleeding pattern
  – **Recent spontaneous or induced bleeding**
    • Continuous sequential
  – **No bleeding for >2-3 cycles**
    • Continuous combined
  – Consider LNG IUC (Mirena, Skyla)...off label use

Continuous P Better Than Sequential

• Oral and transdermal similar risk
• Type of progestin similar risk
• Continuous EP → **76% reduction** in endometrial cancer risk compared to background population
• Sequential EPT
  – 69% risk **elevation** if P was used monthly
  – 276% risk **elevation** if P was used q 3-mos

**Hormone Therapy Dosages**

- Lowest effective ET dose (+ a low P dose if a uterus) consistent with *individual* treatment goals, benefits, and risks
- Lower doses better tolerated, may have more favorable benefit-risk ratio than standard doses
- Additional local ET may be needed for persistent vaginal symptoms


**Hormone Therapy Starting Dosages**

- Lower daily doses typically used with systemic ET
  - 0.3 mg oral CE
  - 0.5 mg oral micronized 17β-estradiol
  - 0.014-0.025 mg transdermal 17β-estradiol patch
- Typical lowest doses of progestogen
  - 2.5 mg oral MPA
  - 0.1 mg oral norethindrone acetate
  - 0.5 mg oral drospirenone
  - 50-100 mg oral micronized progesterone

Choice of Estrogens

- Start *low dose* transdermal or oral ET
- If suboptimal response, modify by
  - Change the estrogen dose (upward)
  - Change the estrogen preparation
  - Change delivery systems (oral → transdermal)
  - Consider an estrogen-androgen combination
- Injectable estrogen not recommended
  - Dosage equivalencies are not known
  - Estrogen cannot be discontinued easily

HT Routes of Administration

- No clear benefit of one route of administration for systemic ET
- Non-oral routes may offer both advantages and disadvantages compared with oral route
- Transdermal ET may be associated with lower DVT risk than oral (observational data, not RCTs)
- Local ET preferred when solely vaginal symptoms

“First Line” Use: Transdermal Estrogen

- Underlying medical conditions
  - History of DVT or PTE
  - High triglyceride levels
  - Gall bladder disease
- Need for “steady state” drug release
  - Daily mood swings (especially while on oral HT)
  - Migraine headaches
- Inability to use oral tablets
  - Stomach upset due to oral estrogen intake
  - Problems with taking a daily pill

Off-Label EPT Uses

- Insufficient endometrial safety evidence to recommend off-label use of...
  - Long-cycle progestogen (every 3-6 mo. for 12-14 days)
  - Vaginal administration of progesterone
  - Levonorgestrel intrauterine system (Mirena®, Skyla®)
  - Low-dose estrogen without progestogen
- Close endometrial surveillance recommended

NAMS position statement. *Menopause*
OCs in Perimenopause

- **Low estrogen** OCs often prescribed because they relieve menopausal symptoms and prevent pregnancy
- Other hormonal methods (patch, ring) may be helpful
- Progestin IUD and DMPA will not address vasomotor symptoms

NAMS position statement. *Menopause 2007*

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Estrogen plus Testosterone

- Moderate to severe VMS not improved by estrogen alone
- Not FDA labelled for improvement of libido
- **Products**
  - Esterified estrogens 1.25 mg + methyltestosterone (MeT) 2.5 mg (Covaryx®XT)
  - Esterified estrogens 0.625 mg + MeT 1.25 mg (Covaryx® H.S.)
  - Previously branded as Estratest
Bazedoxifene 10mg with CE 0.45 mg

- FDA approved tissue selective estrogen receptor modulator (SERM) plus CE
- Progestin-free
- Reduces VMS frequency and severity
- Prevents loss of bone mass
- Treats VVA
- No increase in endometrial hyperplasia
- Amenorrhea, breast tenderness adverse event rates and overall safety similar to placebo

Taylor HS. *Menopause*; 2012 (19);4:479-485.

Compounded Hormone Therapy

- The *marketing* of compounded hormonal therapy
  - Only bioidentical hormones are used
  - Combination of 2 or 3 estrogens is more “natural”
  - Dosage is tailored to the individual
  - More “pure” than commercial products
  - Safer delivery systems (no dyes, etc)
- The *reality*
  - The *same* hormones are used in commercial and compounded 17b-E₂ and progesterone
Compounded Hormone Therapy

Compounded hormones will work about as well as commercial HT products, but...
• Value of adding $E_1 + E_3$ has not been evaluated
• Progesterone skin cream is not absorbed
• Compounded hormone doses are not standardized
• Salivary hormone levels are not useful
• FDA-approved HT products will offer
  – Bioidentical hormones
  – Choice of delivery systems
  – Formulary coverage/ lower out-of-pocket costs

Act 3

Practice Guidelines

*How can your patient use these treatments safely, effectively, and conveniently?*
**Individualization of Therapy**

- An individual risk profile is essential
- Each woman must be informed of her known risks
- Acceptance of HT risks varies with primary indication
- Benefit-risk ratio more acceptable for short-term symptom relief in a younger population
- Long-term HT or use in older women less acceptable
- Women with premature menopause have increased symptoms and risks *if not treated*


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**Treatment of Hot Flashes**

- If mild symptoms, try lifestyle, CAM therapy
- Indications for hormone therapy
  - Moderate or severe symptoms
  - Non-hormonal treatments have failed
  - No interest in non-hormonal therapy
- Titrate estrogen dosage upward *if needed*
- When estrogen can’t be used, offer
  - SSRI or SNRI
  - Gabapentin, clonidine, a-methyldopa
  - Progestins alone
- **Attempt discontinuation after 2 years**
Treatment of Sleep/ Irritability Symptoms

- If mild symptoms
  - Lifestyle change, CAM therapy
- If severe symptoms or no response to above
  - Low dose HT, then titrate upward
  - If mood swings, transdermal E preferred
- Depression component, or no response to HT
  - SSRI; sedating best is (paroxetine)
  - SNRI; venlafaxine

Treatment: Sleep Hygiene

- **Environment**
  - Minimize noise and light
  - Room temperature; keep room cool
- **Diet**
  - Less food late in the day
  - Less fluid before bed
- **Exercise; more regular and earlier in the day**
- **Less caffeine consumption, none past noon**
- **Less alcohol consumption**
Menopausal Vaginal Thinning

- Dryness
- Discharge/vaginitis
  - Yellow creamy
  - Bloody
- Spotting or bleeding
- Dyspareunxia
  - Decreased lubrication
  - Less vaginal elasticity
  - Skin irritation


HT and Vaginal Thinning

- OTC vaginal lubricants often improve vaginal dryness and painful intercourse...first line therapy
  - “Intimate lubricant” (with silicon) for sex
  - Vaginal moisturizer, for times other than sex
- When HT is considered solely for this indication, local (not systemic) vaginal ET is recommended
- Progestogen generally *not indicated* with low-dose, local vaginal ET

Ospemiphene (Osphena)

- Nonhormonal selective estrogen-receptor modulator (SERM)
  - Estrogen agonist/antagonist
  - Tissue selective effects.
  - Only SERM approved in the United States to treat moderate to severe dyspareunia
- 60mg oral dose

HT & Sexual Function

- Treatment of moderate to severe vaginal atrophy with systemic ET/EPT or local ET can relieve dyspareunia
- One oral systemic ET product FDA is approved for dyspareunia
- HT is not recommended as sole treatment of other sexual function problems (e.g., diminished libido)

HT and “Quality of Life”

• RCTs and retrospective studies show that HT has no effect on “quality of life” measures
• Many woman who wean from HT state that they “feel worse”...even after 20 years after menopause!
• Conventional wisdom
  – In women who “feel better on/ worse off” of HT, continue low dose HT if few or no risk factors
  – When (& how often) to re-attempt wean uncertain
  – Don’t start HT for solely for improving QOL

Act 4

The Finale
HT Discontinuance and Symptom Recurrence

- After 2 years of use, recommend drug vacation to determine whether HT is still needed
- Vasomotor symptom recurrence similar whether tapered or abrupt discontinuance
  - 25-50% chance of symptoms recurring when HT discontinued
- Decision to resume HT must be individualized


A decade after the Women's Health Initiative—the experts do agree


*Fertility and Sterility* Aug 2012; 98 (2):313-14

Endorsed by 15 medical associations

- Systemic HT is an acceptable option for healthy women up to age 59 or <10 years of menopause and who are bothered by moderate to severe menopausal symptoms
- Individualization is key in the decision to use HT
- Consider quality-of-life priorities as well as her personal risk factors
Global Consensus Statement on Menopausal Hormone Therapy
T. J. de Villiers et al, Climacteric 2013;16:203–204

- MHT is the most effective treatment for vasomotor symptoms
- Benefits more likely to outweigh risks for symptomatic women < 60 y.o. or < 10 years after menopause
- MHT is effective for prevention of osteoporosis-related fractures in at-risk women < 60 y.o. or < 10 years after menopause

Global Consensus Statement on MHT

- In women with premature ovarian insufficiency, systemic MHT is recommended at least until the average age of the natural menopause
- The use of custom-compounded bioidentical hormone therapy is not recommended
- Current safety data do not support the use of MHT in breast cancer survivors
Appendix

Global Consensus Statement on MHT

- The risk of VTE and ischemic stroke increases with oral MHT but the absolute risk is rare below age 60 years
  - Lower risk with transdermal therapy
- Use of MHT is an individual decision in terms of quality of life, as well as personal risk factors such as age, time since menopause and the risk of VTE, stroke, ischemic heart disease and breast cancer
### Estrogen Dose Equivalents

17-β-estradiol ($E_2$) is the only formulation considered bioidentical*.

<table>
<thead>
<tr>
<th>Estrogen</th>
<th>Standard</th>
<th>Low Dose</th>
<th>Ultra-Low Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Conjugated equine estrogen (CEE)</td>
<td>0.625</td>
<td>0.3</td>
<td></td>
</tr>
<tr>
<td>Oral $E_2$</td>
<td>1mg</td>
<td>0.5mg</td>
<td></td>
</tr>
<tr>
<td>Transdermal $E_2$</td>
<td>0.05mg</td>
<td>0.025mg</td>
<td>0.014 mg</td>
</tr>
<tr>
<td>Ethinyl estradiol</td>
<td>5mcg</td>
<td>0.025mg</td>
<td></td>
</tr>
</tbody>
</table>

*2007 Position Statement of the Endocrine Society.

### ET Oral Tablets

<table>
<thead>
<tr>
<th>Product</th>
<th>Brand</th>
<th>Standard dose</th>
<th>Low dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Conjugated equine estrogen</td>
<td>Premarin</td>
<td>0.625 mg</td>
<td>0.3, 0.45 mg</td>
</tr>
<tr>
<td>Conjugated estrogen (synth)</td>
<td>Cenestin Enjuvia</td>
<td>0.625 mg</td>
<td>0.3, 0.45 mg</td>
</tr>
<tr>
<td>Esterified estrogen</td>
<td>Menest Estratab</td>
<td>0.625 mg</td>
<td>0.3 mg</td>
</tr>
<tr>
<td>Product</td>
<td>Brand</td>
<td>Standard dose</td>
<td>Low dose</td>
</tr>
<tr>
<td>------------------</td>
<td>----------------</td>
<td>---------------</td>
<td>----------</td>
</tr>
<tr>
<td>Estropipate</td>
<td>Ogen</td>
<td>0.625 m</td>
<td>none</td>
</tr>
<tr>
<td></td>
<td>Ortho-est</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Generic</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Micronized $E_2$</td>
<td>Estrace</td>
<td>1.0 mg</td>
<td>0.5 mg</td>
</tr>
<tr>
<td></td>
<td>Generic</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Estradiol acetate</td>
<td>Femtrace</td>
<td>0.9 mg</td>
<td>0.45 mg</td>
</tr>
</tbody>
</table>

**ET Oral Tablets (continued)**

**ET Transdermal: Patch***

<table>
<thead>
<tr>
<th>Brand name</th>
<th>Mg/24 hr</th>
<th>Use/ wk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alora</td>
<td>0.025, 0.05, 0.075, 0.1</td>
<td>2</td>
</tr>
<tr>
<td>Esclim</td>
<td>0.025, 0.0375, 0.05, 0.075, 0.1</td>
<td>2</td>
</tr>
<tr>
<td>Estraderm</td>
<td>0.05, 0.1</td>
<td>2</td>
</tr>
<tr>
<td>Vivelle</td>
<td>0.05, 0.1</td>
<td>2</td>
</tr>
<tr>
<td>Vivelle-Dot</td>
<td>0.025, 0.0375, 0.05, 0.075, 0.1</td>
<td>2</td>
</tr>
<tr>
<td>Climara</td>
<td>0.025, 0.0375, 0.05, 0.06, 0.075, 0.1</td>
<td>1</td>
</tr>
<tr>
<td>Menostar</td>
<td>0.014 ☼</td>
<td>1</td>
</tr>
</tbody>
</table>

* All contain 17B-estradiol only
☢ Indicated only for prevention of osteoporosis
### ET Transdermal: Gels, Emulsions, Sprays*

<table>
<thead>
<tr>
<th>Brand name</th>
<th>Type</th>
<th>mg/24 hr</th>
<th>Use</th>
</tr>
</thead>
<tbody>
<tr>
<td>Divigel</td>
<td>Gel</td>
<td>0.25, 0.5, 1 mg/packet</td>
<td>1 packet daily</td>
</tr>
<tr>
<td>Elestrin</td>
<td>Gel</td>
<td>0.87 gm pump</td>
<td>1 pump daily</td>
</tr>
<tr>
<td>EstroGel</td>
<td>Gel</td>
<td>1.25 gm pump</td>
<td>1 pump daily</td>
</tr>
<tr>
<td>Estrasorb</td>
<td>Emulsion</td>
<td>1.74 gm/pouch</td>
<td>2 pouches daily</td>
</tr>
<tr>
<td>Evamist</td>
<td>Spray</td>
<td>1.53 mg/spray</td>
<td>1 spray daily</td>
</tr>
</tbody>
</table>

* All contain 17B-estradiol only

### Progesterone/ Progestin Products

<table>
<thead>
<tr>
<th>Oral Progestin</th>
<th>Equiv dose</th>
<th>Available doses</th>
</tr>
</thead>
<tbody>
<tr>
<td>MPA</td>
<td>5-10 mg</td>
<td>1.2, 2.5, 5, 10 mg</td>
</tr>
<tr>
<td>Micronized progesterone</td>
<td>200-300 mg</td>
<td>100, 200 mg</td>
</tr>
<tr>
<td>Drospirenone</td>
<td>0.5 mg/d</td>
<td>0.5 mg/d</td>
</tr>
<tr>
<td>Norethindrone acetate</td>
<td>1.0 mg/d</td>
<td>0.5, 1.0 mg/d</td>
</tr>
<tr>
<td>Norethindrone</td>
<td>0.7-1.0 mg/d</td>
<td>0.35 mg</td>
</tr>
<tr>
<td>Norgestimate</td>
<td>0.09 mg</td>
<td>0.09 mg</td>
</tr>
<tr>
<td>Norgestrel</td>
<td>150 mcg/d</td>
<td>150 mcg/d</td>
</tr>
</tbody>
</table>
### EPT Oral Tablets

<table>
<thead>
<tr>
<th>Brand</th>
<th>Estrogen</th>
<th>Progestin</th>
<th>Dosing</th>
</tr>
</thead>
<tbody>
<tr>
<td>Activella</td>
<td>17β-E2 1 mg</td>
<td>NETA 0.5 mg</td>
<td>Once daily oral</td>
</tr>
<tr>
<td>Angeliq</td>
<td>17β-E2 1 mg</td>
<td>Drosperinone 0.5 mg</td>
<td>Once daily oral</td>
</tr>
<tr>
<td>FemHRT</td>
<td>EE 5 µg EE 2.5 µg</td>
<td>NETA 1 mg NETA 0.5 mg</td>
<td>Once daily oral</td>
</tr>
<tr>
<td>Prefest</td>
<td>17β- E2 1 mg</td>
<td>NGM 0.09 mg</td>
<td>E 3 days, E+P 3 days</td>
</tr>
<tr>
<td>Premphase 14 active 14 placebo</td>
<td>CEE 0.625 mg</td>
<td>MPA 5 mg</td>
<td>Once daily oral (CS-EPT)</td>
</tr>
<tr>
<td>Prempro 28 active</td>
<td>CEE 0.625 mg 0.45 mg 0.3 mg</td>
<td>MPA 5.0 mg; 2.5 mg 2.5 mg 1.5 mg</td>
<td>Once daily oral (CC-EPT)</td>
</tr>
</tbody>
</table>

### EPT Transdermal Patches

<table>
<thead>
<tr>
<th>Brand</th>
<th>Estrogen</th>
<th>Progestin</th>
<th>Dosing</th>
</tr>
</thead>
<tbody>
<tr>
<td>CombiPatch</td>
<td>17β-E2 0.05 mg 0.05 mg</td>
<td>NETA 0.14 0.25 mg</td>
<td>Twice weekly</td>
</tr>
<tr>
<td>Climara Pro</td>
<td>17β-E2 0.045 mg</td>
<td>LNG 0.015 mg</td>
<td>Once weekly</td>
</tr>
</tbody>
</table>
### Vaginal Estrogen Therapies

<table>
<thead>
<tr>
<th>Product</th>
<th>Brand</th>
<th>Dosage</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Conjugated estrogen cream</td>
<td>Premarin cream</td>
<td>0.625 mg/gram</td>
<td>Daily, then 1-3 time/wk</td>
</tr>
<tr>
<td>Estradiol cream</td>
<td>Estrace</td>
<td>0.01% (0.1 mg/gm)</td>
<td>Daily, then 1-3 time/wk</td>
</tr>
<tr>
<td>Estradiol vaginal tablet</td>
<td>Vagifem</td>
<td>25 micrograms</td>
<td>Daily for 2 wks, BIW</td>
</tr>
<tr>
<td>Estradiol ring</td>
<td>Estring</td>
<td>7.5 mcg/24 hrs</td>
<td>Every 90 days</td>
</tr>
<tr>
<td>Estradiol ring*</td>
<td>Femring</td>
<td>0.05 mg/d 0.1 mg/d</td>
<td>Every 3 months</td>
</tr>
</tbody>
</table>

*Intended to be used as systemic HT

### Topical Vaginal Estrogen

<table>
<thead>
<tr>
<th>Composition</th>
<th>Brand Name</th>
<th>Dose and sig</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vaginal cream 17β-Estradiol</td>
<td>Estrace Vaginal Cream</td>
<td>Initial: 2.0-4.0g/d for 1-2 wk Maintenance: 1.0g/d (0.1 mg/g)</td>
</tr>
<tr>
<td>Vaginal cream conjugated estrogens</td>
<td>Premarin Vaginal Cream</td>
<td>0.5-2.0 g/d or twice/wk (0.625 mg/g) Use lowest effective dose</td>
</tr>
<tr>
<td>Vaginal ring 17β-estradiol</td>
<td>Estring®</td>
<td>Ring contains 2 mg releases 7.5 mcg/d for 90 d</td>
</tr>
<tr>
<td>Vaginal ring Estradiol acetate</td>
<td>Femring® (Systemic dose and indication)</td>
<td>Systemic dose ring for 90 d 12.4mg releases 50mcg/d 24.8mg releases 100mcg/d</td>
</tr>
<tr>
<td>Vaginal tablet Estradiol hemihydrate</td>
<td>Vagifem® 10mcg (25mcg no longer available)</td>
<td>Initial: 1 tablet/d for 2 wk Maintenance: 1 tab 2x /wk</td>
</tr>
</tbody>
</table>